REMARKS

The finality of the restriction requirement is noted. Applicants confirm their election of Group I, and request that non-elected claim 14 be maintained in this Application, without further action, for possible rejoinder and/or for filing of a divisional application.

With regard to the objection to claim 12, it is unclear as to what the Examiner finds objectionable about claim 12 since claim 12 is believed to further limit claim 1. Nevertheless, in the interest of expediting allowance of the subject Application, Applicants have cancelled claim 12.

Turning to the rejection of the claims under 35 U.S.C. 112, Second Paragraph, with regard to item 3A, the Examiner objected to the use of the term "weighting factors" in claim 1, in contrast to the "weight factors" used in the description. Applicants note that these terms mean the same. Notwithstanding, claim 1 has been amended to avoid confusion. Occurrences of the word "weighting" have also been amended in claims 2 and 15.

With regard to item 3B, the Examiner has alleged that the "energy function being a sum" wording is not clear and is not consistent with the description. Applicants have amended claim 1 to read more precisely and consistently with the description, as "said energy function being a linear combination of energy parameters, with weight factors, as coefficients." For example, if A, B, C are energy parameters and $c1$, $c2$, $c3$ are weight factors, then the energy function has the form: $c1*A + c2*B + c3*C$.

With regard to item 3C, the Examiner has alleged that there is no support for the step of "determining values for weighting factors" in claim 1. Applicants submit that a person skilled in the art and familiar with the body of academic work in the field would be aware of several different methods to determine the weight factors. The present Patent Application does not

describe any advancement in this specific area, and in fact, Applicants' commercial product, the RAPTOR software, uses known weight factors for the scoring function.

One example of a system to determine acceptable weight factors is described in the paper cited by the Examiner: Meller et al. Proteins: Structure, Function, and Genetics, 2001, Volume 45, Issue 3, Pages 241-261. As Applicants will reiterate upon hereinafter, the contribution of Meller et al. is precisely at the step of generating weight factors using LP, and it goes no further than this (i.e., it has nothing to do with the use of LP for threading, as per the claimed invention).

As noted in the abstract of their paper, Meller et al. stated clearly: "To design optimal scoring functions we use linear programming (LP)." The "scoring function" described by Meller et al. could be used as one of the "energy functions" described in the subject Patent Application, though Applicants have not used Meller et al.'s particular scoring function. The use of any specific scoring function is not claimed as part of the invention.

To avoid giving the impression that the invention teaches a new way of determining weight factors, Applicants have removed the step of "determining..." from claim 1.

With regard to item 3D, the Examiner has noted a difficulty with antecedent basis in claim 3. Applicants submit that the amendment to claim 1 makes claims 1 and 3 consistent with one another, thereby addressing the Examiner's concern.

With regard to item 3E, the Examiner has asked that claims 8-10 incorporate the specific wording of each of the constraints that they refer to. Applicants have amended these claims accordingly, relying on the text of the description from pages 10 and 11.

Turning to the rejection of the claims under 35 U.S.C. 101, in the interest of expediting the Application to allowance, Applicants have amended the two independent claims 1 and 15 to

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explicitly recite the identification of a "best fit" between the query protein sequence and the template. Providing this data as a specific output should provide the practical result that the Examiner is seeking.

The claimed invention is very useful in the pharmaceutical industry. It allows one to compare a protein sequence to a known set of pre-selected protein structures and identify potential drug targets (i.e., the "best fit"). Hence, this is a very useful tool for drug design, and certainly meets the standards for "tangible result" and "practical application."

Turning the to rejection of the claims based on the art, considering first the rejection of claims 1, 2 and 15 as anticipated by Meller et al. Applicants submit that the Meller et al. paper does not deal with the same problem as the claimed invention, nor does it describe the combination of features of claims 1, 2 or 15.

The abstract of the Meller et al. paper very clearly sums up their paper: "To design optimal scoring functions we use linear programming (LP)." The Meller et al. paper is about designing optimal scoring functions using linear programming and it does not go any further than that – i.e., they do not describe the use of linear programming to perform actual protein threading.

Applicants use linear programming for a completely different mathematical problem: how to optimally fit a protein sequence onto a protein structure, under a *given* energy function (or scoring function). Applicants indeed use a given scoring function and it can even be Meller et al.'s scoring function – this is referred to as an energy function in the subject Patent Application. The claimed invention finds the best ways to "thread" a query sequence to existing structures using linear programming – a completely different process.

Linear programming is a very common mathematical tool like calculus and algebra. So it is expected to find it used elsewhere in the field of bioinformatics. However, Meller et al. is using linear programming to deal with a completely different problem, and the fact that linear programming is useful for generating energy functions does not suggest that it will be useful at all in threading protein query sequences to existing structures. These are completely different and unrelated problems.

Thus, Meller et al. cannot be said to teach claims 1, 2 or 15, and the rejection of claims 1, 2 and 15 as anticipated by Meller et al. is in error.

Turning to the rejection of claims 3-7, 11 and 13 as obvious from Meller et al. in view of Akutsu et al., claims 3-7, 11 and 13 are all dependent on claim 1. The deficiencies of primary reference Meller et al. vis-à-vis claim 1 are discussed above. It is not seen that the secondary reference to Akutsu et al. supplies the missing teachings to Meller et al. to achieve or render obvious claim 1 or any of the claims dependent thereon. The Akutsu et al. paper merely proves that protein threading is MAX SNP-hard, which means that it falls into a certain class of problems in computational complexity theory. The Akutsu et al. paper does not explain how to use linear programming and known energy functions to thread protein query sequences to existing structures.

Furthermore, Applicants submit that the Akutsu et al. paper serves to support the claimed invention. The Akutsu et al. paper proves that the problem of the invention is very hard to solve, which speaks to the ingenuity and importance of the claimed invention. Thus, neither the Akutsu et al. paper nor the Meller et al. paper deal with the problem of the invention, much less provide a solution. Clearly, the person skilled in the art would *not* be led to the claimed invention by considering these two papers, and no combination of Meller et al.
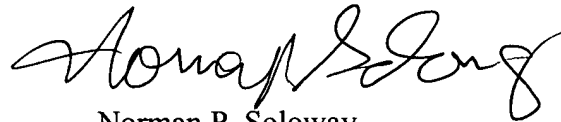
and Akutsu et al. would achieve or render obvious claim 1 or any of the claims dependent

thereon.

Finally, the rejection of claim 12 is obvious from Meller et al. in view of Ding et al. has

been rendered moot by cancellation of that claim.

Having dealt with all the objections raised by the Examiner, the Application is believed

to be in order for allowance. Early and favorable action are respectfully requested.

In the event there are any fee deficiencies or additional fees are payable, please charge

them (or credit any overpayment) to our Deposit Account Number 08-1391.

Respectfully submitted,

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